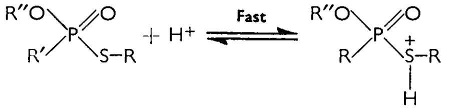
905. *The Concerted Action of Fluoride and Silver Ions on Diethyl Ethylphosphonothiolate in Aqueous Solution.*

By B. SAVILLE.

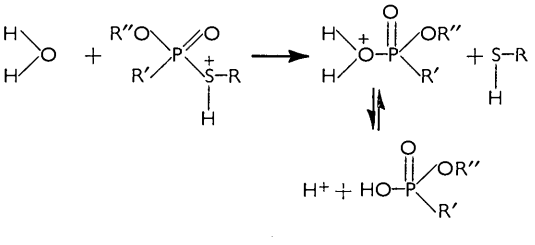
The hydrolysis of phosphonothiolate esters in neutral or acid solution, and the substitution reaction with fluoride ion, represented, $H_2O + RO{\cdot}PR(:O){\cdot}SR \longrightarrow HO{\cdot}PR(:O){\cdot}OR + RSH$, $F^- + RO{\cdot}PR(:O){\cdot}SR \longrightarrow F{\cdot}PR(:O){\cdot}OR + RS^-$, normally occur slowly. It is now shown that silver ions exert a powerful assistance in nucleophilic displacements of this type, high yields of ethyl ethylphosphonofluoridate being obtained, under mild conditions, in this way (second reaction).

Some kinetic measurements have been made concerning these assisted reactions for which mechanistic propositions are advanced.

THE hydrolysis in acid solution of phosphonothiolic esters $R''O{\cdot}PR'(:O){\cdot}SR$ has not been studied in detail, but if hydrogen-ion catalysis is assumed to operate, as is suggested by results on analogous reactions,[1,2] it appears that the probable reaction mechanism is:



. . . . (i)



. . . . (ii)

According to this scheme the phosphonothiolate ester reacts in equilibrium with hydrogen ions to yield a low concentration of a protonated intermediate which by virtue of its considerably weakened P–S bond suffers nucleophilic attack at the phosphorus atom by the solvent (water) molecules, expelling the thiol group.

Qualitatively, it is known that the catalytic effect of hydrogen ions is small compared with that of hydroxyl ions, and that the rate of hydrolysis of phosphonothiolates even in strong mineral acid is so low that high temperatures are required to bring the reaction to a conveniently measurable rate. The low reactivity of the nucleophilic solvent towards phosphonothiolates, even in strongly acid solution, may reflect the very low degree of protonation of the sulphur atom in the sense of equation (i). This postulate seems plausible on the basis that sulphur is much less basic than oxygen towards hydrogen ions and other

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[1] Hudson and Keay, *J.*, 1956, 3269.

[2] Ripper, 3rd Internat. Congr. Crop Protection, Paris, 1952. Reported in " Organic Insecticides," Metcalf, Interscience, New York, 1955.

highly positive centres, as indicated, for example, by the much higher dissociation constants of thiols than of the corresponding alcohols.

On the other hand, derivatives of bivalent sulphur can co-ordinate very powerfully with certain atomic centres, a phenomenon particularly well displayed in the case of mercuric and silver ions. A review[3] of ligand–acceptor affinities comments on the sequence $S \gg O$ for bonding with Ag^+. Accordingly, if the sulphur atom of a phosphonothiolate ester molecule were to co-ordinate with either mercuric or silver cations the P–S bond ought to be considerably weakened by interatomic repulsion so that the susceptibility of the phosphorus atom towards attack by nucleophiles would be enhanced. Thus the hydrolysis, alcoholysis, etc., of phosphonothiolates should be markedly catalysed by metal cations or other substances having a high affinity for sulphur.

The literature gives little information on such possible catalytic effects. Emmett and Jones,[4] however, when seeking a test to distinguish trimethyl phosphorothiolate $MeS{\cdot}P(O)(OMe)_2$ from the thiono-isomer $P(S)(OMe)_3$, found that aqueous or alcoholic silver nitrate gave with the former a precipitate having the approximate composition $(AgSMe)_2,AgNO_3$. This has been checked for triethyl phosphorothiolate, similar qualitative results being obtained. Since this reaction obviously indicates that silver ions assist nucleophilic attack on phosphorus and displacement of the thiol grouping by water, it was considered that the rate of attack by other nucleophilic reagents should be similarly enhanced.

The reaction between fluoride ions and diethyl ethylphosphonothiolate was used to test this prediction. Normally, this reaction in aqueous solution gives no phosphonothiolate decomposition during several days, but if silver ions were effective in assisting the displacement it would be a simple matter[5] to recognise the ethyl ethylphosphonofluoridate which would be formed thus: $F^- + EtO{\cdot}PEt(O){\cdot}SEt + Ag^+ \longrightarrow F{\cdot}PEt(O){\cdot}OEt + AgSEt$. Fluoride ion was chosen as the nucleophile to compete with water for the phosphonothiolate because it is known to possess a high reactivity towards reactive organophosphorus compounds, *e.g.*, phosphorochloridates,[6] and because the ion does not form a complex or a precipitate with silver ions in aqueous solution.

Experiment verified the predictions.

EXPERIMENTAL

Materials.—Inorganic materials were of " AnalaR " grade or of the best available purity. Diethyl ethylphosphonothiolate, prepared by Dr. B. C. Barrass (C.D.E.E., Porton), had b. p. 67—68°/2 mm., n_D^{25} 1·4725 (lit.,[7] b. p. 76·5°/4 mm., n_D^{20} 1·4730).

The reaction of mixed sodium fluoride–silver nitrate solution with diethyl ethylphosphonothiolate was performed in a fume cupboard, and apparatus was decontaminated with aqueous sodium hydroxide solution. Diethyl ethylphosphonothiolate (18·2 g., 0·1 mole) was added to sodium fluoride (6·3 g., 0·15 mole) in water (300 ml.), followed during 10 min. with stirring, by silver nitrate (25·5 g., 0·15 mole) in water (100 ml.). A white precipitate was deposited, and after a further 10 min. sodium chloride (10 g.) in water (50 (ml. was added to precipitate the excess of silver, the mixture was filtered under suction, and the precipitate was washed with water (100 ml.). The combined filtrate and washings were extracted with chloroform (3 × 50 ml.), and the extracts dried and distilled, affording crude *ethyl ethylphosphonofluoridate* (N.B.: extremely poisonous), b. p. 157—158°/760, 55—56°/11 mm. (11 g.), which, on redistillation, gave a pure ester, b. p. 24°/1·5 mm., n_D^{25} 1·3860 (Found: C, 34·9; H, 7·6; F, 13·4. $C_4H_{10}FO_2P$ requires C, 34·3; H, 7·2; F, 13·6%).

The precipitate was suspended in an excess of aqueous ammonia (to dissolve the halide), filtered off, and washed with dilute ammonia, water, and finally acetone before vacuum-drying to yield a silver ethyl sulphide nitrate (24 g.), m. p. 300° (Found: C, 7·7; H, 1·9; S, 9·2; Ag,

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[3] Ahrland, Chatt, and Davies, *Quart. Rev.*, 1958, **12**, 265.

[4] Emmett and Jones, *J.*, 1911, **99**, 713.

[5] Marsh and Neale, *Chem. and Ind.*, 1955, 494.

[6] Dostrovsky and Halmann, *J.*, 1953, 508.

[7] Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1953, 163; *Chem. Abs.*, 1954, **48**, 3244.

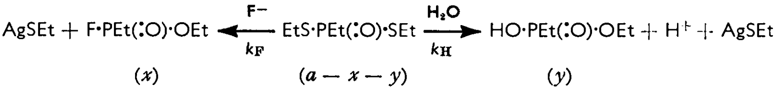
63·3. Calc. for $C_2H_5SAg,AgNO_3$: C, 7·1; H, 1·5; S, 9·5; Ag, 63·7%). It was insoluble in organic solvents, dilute nitric acid, and ammonia, but dissolved in an excess of sodium cyanide solution with the liberation of ethanethiol.

Hydrolysis of Diethyl Ethylphosphonothiolate in the Presence of Silver Ions.—The ester (0·1 mole) in water (100 ml.) was added to silver nitrate (0·2 mole) in water (200 ml.). A precipitate (25 g.), as above, was formed and after 20 min. sodium chloride (10 g.) in water (50 ml.) was added. The mixture was filtered and the precipitate washed with water before the filtrate and washings were made up to 1 l. with water. Titration with 0·1N-sodium hydroxide (phenolphthalein) indicated that 1·0 mole of diethyl ethylphosphonothiolate afforded 1·97 moles of acid, in accordance with the expectation that one mole of ethyl ethylphosphonic acid and one mole of nitric acid would be finally produced.

Kinetics of Decomposition of Diethyl Ethylphosphonothiolate in Aqueous Silver Nitrate–Sodium Fluoride Systems.—Appropriate volumes of concentrated stock solutions of sodium fluoride and silver nitrate were mixed, and they were diluted with water or sodium nitrate solutions whereby constant ionic strength was maintained. The mixtures, in flasks blackened to minimise photochemical action, were brought to the required temperature. Small volumes of concentrated aqueous diethyl ethylphosphonothiolate were added to give an initial ester concentration of about 0·001M. At convenient times aliquot parts (5 ml.) were withdrawn and added to N-potassium chloride (1 ml.) to precipitate the excess of silver, thereby stopping the reaction. The solutions were then filtered through Whatman No. 1 papers, and the filtrates (1 ml.) added to the dianisidine–peroxide reagent,[5] giving coloured solutions the intensities of which were independently found to be directly proportional to phosphonofluoridate concentration. Other experiments had shown that this colorimetric method suffers no interference from residual phosphonothiolate.

Another colorimetric procedure was also employed for the determination of residual phosphonothiolate in the filtrate. This does not suffer interference by phosphonofluoridate and was therefore suitable for following kinetically phosphonothiolate hydrolyses at the lower silver ion concentrations. To the filtrate (1 ml.) were added bromine water (1 ml.) (1 vol. of saturated aqueous bromine + 19 vol. of water), and after 1 min. 2% phenol–5% potassium bromide solution (1 ml.) in water; the whole was mixed, and pyridine–benzidine–cyanide reagent * added to a total volume of 10 ml. The intensity of the red colour developed after 15—20 min. was compared with that of a control, 1 cm. cells and Ilford 604 filters on a Hilger absorptiometer being used. There was a linear relation between phosphonothiolate concentration (0·00001—0·00012M) and absorptiometer readings. The method depends on the formation of ethanesulphonyl bromide [8] by the action of aqueous bromine on the phosphonothiolate, and the conversion of cyanide by the sulphonyl bromide [9] into cyanogen bromide which produces a red dye with pyridine and benzidine.

Treatment of Kinetic Data.—Suppose that in the presence of constant silver ion concentration the measured reactions may be represented:



$$\underset{(x)}{\text{AgSEt} + \text{F·PEt(:O)·OEt}} \xleftarrow[k_F]{F^-} \underset{(a-x-y)}{\text{EtS·PEt(:O)·SEt}} \xrightarrow[k_H]{H_2O} \underset{(y)}{\text{HO·PEt(:O)·OEt}} + H^+ + \text{AgSEt}$$

Here, a is the initial phosphonothiolate concentration, x and y are the concentrations, at time t, of phosphonofluoridate and phosphonic acid formed in the reaction, and k_H and k_F are the first-order rate constants. The initial concentrations are always $(F^-) \gg a \ll (Ag^+)$.

It follows from the theory of competing first-order reactions that

$$y = xk_H/k_F. \tag{1}$$

The rate of phosphonofluoridate formation is given by

$$dx/dt = k_F[\text{Phosphonothiolate}] = k_F(a - x - y). \tag{2}$$

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* This reagent is prepared by mixing 5 volumes of pyridine–hydrochloric acid (Aldridge, *Analyst*, 1945, **70**, 474) with 1 volume of 5% benzidine hydrochloride in 3% hydrochloric acid and 1 volume of 1% potassium cyanide. It may be used up to 2 hr. after being prepared.

[8] Stirling, *J.*, 1957, 3597.

[9] Saville, *Chem. and Ind.*, 1956, 660.

Substituting (1) in (2), one obtains

$$dx/dt = k_F[a - x(k_F + k_H)/k_F]$$

which rearranges to

$$dx/dt = (k_F + k_H)[ak_F/(k_F + k_H) - x]. \tag{3}$$

It may also be shown that on completion of the reaction the final value of x is $ak_F/(k_F + k_H)$, so that equation (3) becomes $dx/dt = (k_F + k_H)(x_\infty - x)$, which integrates to

$$\log_e [x_\infty/(x_\infty - x)] = (k_F + k_H)t.$$

Hence a plot of $\log_{10} (x_\infty - x)$ against t gives a straight line whose negative slope equals 1/2·303 of the sum of the rate constants k_F and k_H. (This treatment neglects aqueous hydrolysis of the phosphonofluoridate. This was studied and found to be a first-order process of *ca.* 8 hr. half-life, *i.e.*, very much slower than the processes being studied here.)

The variation of k_F with fluoride ion concentration can best be examined by plotting the values of $(k_F + k_H)$ (obtained in systems where silver ion concentration is kept constant and fluoride ion concentration varied) against the fluoride ion concentration. It was found in this way that k_F was directly proportional to fluoride ion concentration (Fig. 1), and for Table 1 second-order constants (k_2) have been calculated by dividing k_F by the appropriate fluoride ion concentration. k_F values were obtained by subtracting k_H from $(k_F + k_H)$ after having independently determined k_H at various silver ion concentrations (Table 2).

TABLE 1.

Kinetic results for decomposition of diethyl ethylphosphonothiolate in aqueous silver nitrate–sodium fluoride solutions at 25°.

Phosphonothiolate initially ~0·001M. Total ionic strength 0·2, except where marked with asterisk.

	$[Ag^+]$ (10^{-3} g.-ion/l.)	$[F^-]$ (10^{-2} g.-ion/l.)	$k_H + k_F$ (min.$^{-1}$)	$k_F/[F^-] = k_2$ (l. mole^{-1} min.$^{-1}$)	
	5	0	0·0038 †	—	0·729
	5	5	0·0405	0·734	
	5	10	0·0762	0·724	
	10	0	0·0147 †	—	1·51
	10	2	0·0418	1·36	
	10	4	0·0738	1·48	
	10	8	0·132	1·46	
	10	10	0·165	1·50	
	10	12	0·191	1·47	
	10	19	0·304	1·52	
	20	0	0·056 †	—	4·04
	20	5	0·264	4·16	
	20	10	0·448	3·92	
*	25	0	0·077 †		7·58 *
	25	0·5	0·116	7·80	
	25	1	0·147	7·00	
	25	2·5	0·268	7·56	
	25	5	0·455	7·56	
	25	10	0·830	7·53	
	30	0	0·120 †		8·16
	30	5	0·530	8·20	
	30	10	0·932	8·12	
	40	0	0·191 †		
	40	10	1·38	11·9	11·9
	50	0	0·289 †		
	50	10	2·06	17·7	17·7

* No addition of $NaNO_3$, so that ionic strength was variable. † These values are k_H.

TABLE 2.

Rates of hydrolysis of diethyl ethylphosphonothiolate in aqueous silver nitrate–sodium nitrate solutions at 25°. (The ionic strengths were varied by addition of sodium nitrate.)

$[Ag^+]$ (10^{-3} g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)	$[Ag^+]$ (10^{-3} g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)	$[Ag^+]$ (10^3 g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)
5	0·200	0·0038 *	20	0·500	0·0633	50	0·050	0·228
10	0·200	0·0146 *	25	0·025	0·0600	50	0·200	0·289 *
20	0·020	0·0414	30	0·200	0·120 *	100	0·100	0·863
20	0·200	0·0560 *	40	0·200	0·191 *			

* Strictly comparable on an equal-ionic-strength basis.

DISCUSSION

The following facts emerge from the kinetic examination: (i) For the simple phosphonothiolate hydrolysis, the first-order rate constants, k_H, are fairly accurately proportional to the square of the silver ion concentration at constant ionic strength. (ii) The rates of ester substitution by fluoride ion are directly proportional to the concentration of fluoride ion at a given $[Ag^+]$ (Fig. 1). (iii) The kinetic order with respect to silver ions for the fluoride ion substitution varies from near unity at low $[Ag^+]$ to a value approaching two at higher concentrations.

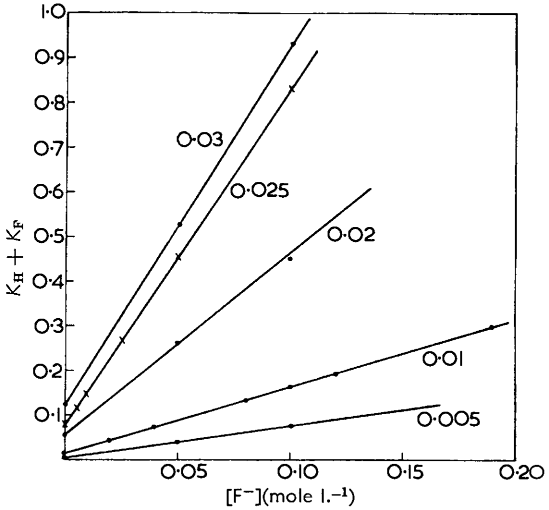
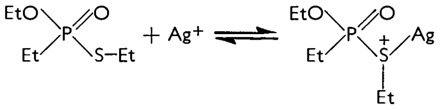


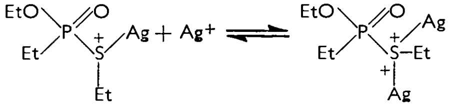
FIG. 1. Relation between first-order rate constants for diethyl ethylphosphonothiolate decomposition and fluoride ion concentration at various silver ion concentrations.

Silver concentrations (g.-ion l.$^{-1}$) are given against appropriate curve; ● ionic strength = 0·2; × ionic strength variable = 0·025 + $[F^-]$.

These results are accommodated if the ester is involved in stepwise co-ordination equilibria with silver ions, yielding small concentrations of the argentated intermediates (I) and (II) which are then susceptible to nucleophilic attack by solvent or fluoride ions:



(I) . . . . (iii)



(II) . . . . . . (iv)

$$\text{(I)} + H_2O \longrightarrow EtO{\cdot}PEt(\text{:}O){\cdot}OH + H^+ + AgSEt \qquad \text{(v)}$$

$$\text{(I)} + F^- \longrightarrow F{\cdot}PEt(\text{:}O){\cdot}OEt + AgSEt \qquad \text{(vi)}$$

$$\text{(II)} + H_2O \longrightarrow HO{\cdot}PEt(\text{:}O){\cdot}OEt + H^+ + Ag_2SEt^+ \qquad \text{(vii)}$$

$$\text{(II)} + F^- \longrightarrow F{\cdot}PEt(\text{:}O){\cdot}OEt + Ag_2SEt^+ \qquad \text{(viii)}$$

By assuming the equilibria (iii) and (iv) to be established rapidly and the displacements (vi) and (viii) to be relatively slow it is easy to show that the appropriate relation between k_2 and silver ion concentration takes the form

$$k_2 = \alpha[Ag^+] + \beta[Ag^+]^2 \qquad \text{(ix)}$$

where α and β are constants. This expression rearranges to $k_2/[Ag^+] = \alpha + \beta[Ag^+]$, so that a plot of $k_2/[Ag^+]$ against $[Ag^+]$ should be linear. Fig. 2 shows how the present results accord with this analysis. However, as seen already, the hydrolysis is of second order with respect to silver ions, making necessary the conclusion that the monoargentated intermediate (I) is not easily attacked by the moderately nucleophilic water molecules (reaction v) and that the main hydrolytic pathway (vii) occurs dominantly through the intermediate (II). This behaviour is rationalised by postulating that the potently nucleophilic fluoride ion is not especially discriminating with regard to the nature of the leaving groups $-\overset{+}{S}\genfrac{}{}{0pt}{}{\diagup Ag}{\diagdown Et}$, $-\overset{+}{S}\genfrac{}{}{0pt}{}{\diagup Ag}{\genfrac{}{}{0pt}{}{-Et}{\diagdown Ag}}$ of (I) and (II) and so attacks either intermediate, whereas the relatively feeble solvent nucleophiles find it necessary to seek out the intermediate (II) whose P–S bond is particularly weakened.

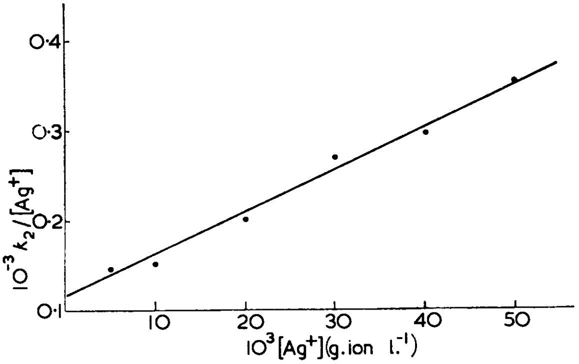
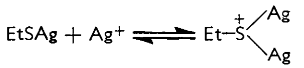


FIG. 2. Experimental test of equation (ix).

The implication from the positive $k_2/[Ag^+]$ intercept at zero $[Ag^+]$ is that fluoride ion can attack a monoargentated ester intermediate (I).

These arguments rest on the existence of equilibria (iii)—(iv). Now whereas (iii) may seem a plausible proposition by analogy with protonation equilibria in oxy-ester chemistry, a process such as (iv), whose existence seem necessary on the present interpretation, requires further comment. For example, the protonation counterpart, $-\overset{+}{O}\genfrac{}{}{0pt}{}{\diagup R}{\diagdown H} + H^+ \rightleftharpoons -\overset{+}{O}\genfrac{}{}{0pt}{}{\diagup H}{\genfrac{}{}{0pt}{}{-R,}{\diagdown H}}$ has not been invoked to explain heterolytic phenomena in strong acids. However, there is evidence that more than one silver ion can co-ordinate with bivalent sulphur: silver ethyl sulphide, normally highly insoluble, dissolves appreciably in concentrated silver nitrate solution, perhaps by a reaction such as


$$EtSAg + Ag^+ \rightleftharpoons Et{-}\overset{+}{S}\genfrac{}{}{0pt}{}{\diagup Ag}{\diagdown Ag} \qquad \text{(III)}$$

giving a soluble salt of the quasi-sulphonium ion (III).* Silver isopropyl methylphosphonothiolate is not appreciably decomposed in water, but it undergoes hydrolysis and

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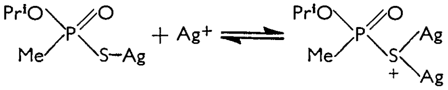
* It has also been found that many insoluble silver derivatives of primary thiols, suspended in tetrahydrofuran, dissolve easily on addition of concentrated aqueous silver perchlorate.

substitution with fluoride ion in the presence of an excess of silver ions. This behaviour seems to require the postulate that further Ag^+ co-ordination occurs, thus:



A simple argument against equilibrium (iv) is the electrostatic improbability of the double positive charge. This objection is removed if the Ag–S bond is covalent, in which case a more even charge distribution over the two atoms would lessen the positivity of the sulphur.

This work was performed during the tenure, at the Chemical Defence Experimental Establishment, Porton, Wilts., of a Civil Service Research Fellowship. The author thanks Dr. C. J. M. Stirling, of Queen's University, Belfast, for much stimulating discussion.

THE NATURAL RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48—56, TEWIN ROAD, WELWYN GARDEN CITY, HERTS.
[*Received, April* 20*th*, 1961.]